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Signed: Douglas E. Reedich Date: 16 November 1994  
Douglas E. Reedich (Reg. No. 33,999)

#8

PATENT

Docket No. 43853USA1D

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

TARLOCHAN S. PUREWAL and  
DAVID J. GREENLEAF

Serial No.: 08/086,820

Filed: July 2, 1993

For: MEDICINAL AEROSOL  
FORMULATIONS

) Examiner: W. Benston, Jr.

) Group Art Unit: 1502

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INFORMATION DISCLOSURE STATEMENT UNDER 37 CFR §1.97(c)

Commissioner of Patents and Trademarks  
Washington, D.C. 20231

This Information Disclosure Statement is submitted as a means for complying with the duty of disclosure set forth in 37 CFR §1.56. Applicants wish to bring to the Examiner's attention the following patents and publications.

U.S. Pat. Nos. 2,885,427  
3,219,533  
3,261,748  
3,897,779  
4,352,789

GB 837,465

Physicians' Desk Reference, 40th Edition 1986,  
Medical Economics Company Inc. at Oradell, NJ

"Comparison of Output Particle Size Distributions from Pressurised Aerosols Formulated as Solutions or Suspensions", R.N. Dalby and P.R. Byron, Pharmaceutical Res., Vol. 5, No. 1 (1988) p. 36

The Theory & Practice of Industrial Pharmacy, Leon Lachman et al., 3rd Ed., Lea & Febiger 1986, Chapter 20, p. 597, 599 and 603

Chemical and Engineering News, 24 November 1986, p. 52

Dupont Update, March 1987

Manufacturing Chemist, May 1988

HFC 134a as a Substitute Refrigerant for CFC 12, H. O. Spauschus, Paper presented 18 to 21 July 1988

Handbook of Aerosol Technology, Second Edition (1979), pp. 30, 32, and 33

Product Information "Les Substituts F 22 - F 502, FC 142b, F 123 - F 134a, FC 141b", Atochem, dated October 1988 (with translation)

Dictionnaire Vidal (1979), pp. 392 - Chibro-Plast-, 1926 - Spray 1000 - and 2239-2240 - Ventoline Aerosol-doseur (with translation)

F. Dorvault "L'Officine" (1978), pp. 547-548 (with translation)

Copy of the product Dexa-Rhinospray sold by C.H. Boehringer Sohn (with translation)

U.S. Senate Hearing, May 12-14, 1987, pp. 487 and 347

The Theory and Practice of Industrial Pharmacy, 2nd Edition, 1976, Lea & Fabiger, Philadelphia, pp. 270 and 276-280

"CFC-Gasser I Medicinske Spray", March 1989, Pedersen et al., pp. 753-755 (with translation)

"CFC Propellant Substitution: International Perspectives", Pharmaceutical Technology International, 1989, Fischer et al., pp. 16-18

Aerosol Age, November 1989, pp. 6, 8

Aerosol Age, November 1989, p. 12

Manufacturing Chemist, November 1989, p. 8

Aerosol Age, November 1989, pp. 16-19

Aerosol Age, November 1989, pp. 24-26

The above-noted patents and publications are listed on the enclosed Form PTO-1449 and a copy of each is enclosed for the Examiner's convenience.

The fee of \$210.00 as required by 37 CFR \$1.17(p) is enclosed herewith. Please charge any additional fees or credit any overpayment to Deposit Account No. 13-3723.

On or about 26 April 1988, two representatives of ICI met with representatives of 3M at 3M's facility in Loughborough, England. The 3M representatives included Tarlochan Purewal and David Greenleaf, inventors in the above-identified application. At that meeting, the ICI representatives disclosed, inter alia, that the compound 1,1,1,2-tetrafluoroethane was under development by ICI as a replacement for a current chlorofluorocarbon refrigerant and that a supply would therefore be available. The ICI representatives also indicated that that compound might be a potential candidate as an aerosol propellant replacement for a current chlorofluorocarbon propellant. Prior to the aforementioned meeting, Mr. Purewal and Mr. Greenleaf had identified the above-mentioned compound as an aerosol propellant suitable for inhalation therapy.

In an August 30, 1988 discussion between representatives of ICI and representatives of 3M, toxicity data concerning HFC 134a and propellant 123 were discussed. The data concerning propellant 123 were deemed less favorable than the data concerning HFC 134a. In a September 1, 1988 discussion between representatives of ICI and representatives of 3M, HFC 134a was identified by ICI as being on the "fastest track" among several candidate refrigerant replacements.

Also, Applicants wish to bring to the Examiner's attention the following commonly assigned copending applications:

U.S.S.N. 07/878,039, filed May 4, 1992, in the names of Robert K. Schultz et al. This application

discloses and claims a pharmaceutical suspension formulation suitable for aerosol administration, comprising a therapeutically effective amount of a micronized drug and a propellant selected from the group consisting of 1,1,1,2-tetrafluoroethane, 1,1,1,2,3,3,3-heptafluoropropane, and a mixture thereof, the formulation being further characterized in that (i) it is substantially free of surfactant, (ii) the drug is readily redispersible, and (iii) upon redispersion the drug does not flocculate so quickly as to prevent reproducible dosing of the drug.

U.S.S.N. 07/769,547, filed October 1, 1991, in the names of Robert K. Schultz et al. This application discloses and claims an aerosol formulation comprising a therapeutically effective amount of beclomethasone 17,21 dipropionate, a propellant comprising a hydrofluorocarbon selected from the group consisting of 1,1,1,2-tetrafluoroethane, 1,1,1,2,3,3,3-heptafluoropropane, and a mixture thereof, and ethanol in an amount effective to solubilize the beclomethasone 17,21 dipropionate in the propellant, the formulation being further characterized in that substantially all of the beclomethasone 17,21 dipropionate is dissolved in the formulation, and that the formulation is free of any surfactant.

U.S.S.N. 07/713,819, filed June 12, 1991, in the names of Robert A. Moris et al. This application discloses and claims a suspension aerosol formulation, comprising: a propellant comprising a hydrofluorocarbon selected from the group consisting of 1,1,1,2-tetrafluoroethane and 1,1,1,2,3,3,3-heptafluoropropane, and a mixture thereof; a therapeutically effective amount of a powdered medicament; and between about 0.001 and 0.6 percent by weight of a dissolved surface-active dispersing agent selected from the group consisting of a perfluorinated sulfonamido alcohol phosphate ester of the formula



wherein  $R_f$  is a perfluorinated radical selected from the group consisting of aliphatic  $C_nF_{2n+1}$  and cycloaliphatic  $C_nF_{2n-1}$  where  $n$  is an integer from about 4 to about 10,  $R$  is selected from the group consisting of hydrogen and alkyl having about 4 to about 12 carbon atoms,  $R'$  is alkylene having about 2 to about 8 carbon atoms and  $m$  is an integer from 1 to 3, and a mixture of two or more of said esters;

the formulation exhibiting substantially no growth in particle size or change in crystal morphology of said medicament over a prolonged period, being substantially readily redispersible, and upon redispersion not flocculating so quickly as to prevent reproducible dosing of the medicament.

U.S.S.N. 07/893,212, filed June 2, 1992, in the names of Robert K. Schultz et al. This application discloses and claims a suspension aerosol formulation comprising an effective amount of a powdered medicament, between about 0.001 and about 0.6 percent by weight of a perfluorinated surface-active dispersing agent, and a propellant comprising a hydrofluorocarbon selected from the group consisting of 1,1,1,2-tetrafluoroethane and 1,1,1,2,3,3,3-heptafluoropropane.

U.S.S.N. 08/026,476, filed March 4, 1993, in the names of Tarlochan S. Purewal et al. This application discloses and claims an aerosol formulation comprising:

(a) a therapeutically effective amount of a medicament; and

(b) a propellant substantially free of chlorofluorocarbons, said propellant comprising 1,1,1,2-tetrafluoroethane,

said formulation being suitable for delivery by oral or nasal inhalation.

Respectfully submitted,

16 November 1994  
Date

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